

Scientific and Technical Information Center

SEARCH REQUEST FORM

256411
 Requester's Full Name: Paula Jais Examine # ██████ Date: 4-3-08
 Alt Unit: 1624 Phone Number: 2-9931 Serial Number: 10593590
 Location (Bldg/Room): 66508 Mailbox #: 0008 Result Format Preferred (circle): PAPER DISK

To ensure an efficient and quality search, please attach a copy of the copy sheet, tables, and abstract or fill out the following:

Title of invention: See Bib Data Sheet

Inventors (please provide full names):

Earliest Priority Date:

Key Words:

Please provide a detailed description of the invention to include the structure, function, and purpose of the invention. Include the chemical structure, if applicable, and the name of the compound. Also include the name of the inventor, the name of the company, and the name of the country. (See examples of key words on the back of this form.)

For Chemical Searches Only Please include all pertinent information (e.g., chemical structure, molecular weight, etc.) along with any appropriate key words.

See class. attached. Please do structure search and inventor name(s) search. Display results to show identification of source, and R.N.#, compound name & structure of identified compounds. Search compound

of Formula I when X is CH with additions as noted

Please call with any questions

STAFF USE ONLY

Type of Search

Yields and cost where applicable

Searcher's Name:

By: Shawna M.

Yield:

Cost:

Searcher's Title:

AA Jones (M)

Yield:

Cost:

Searcher's Name:

Shawna M.

Yield:

Cost:

Date Search Requested:

By: Shawna M.

Yield:

Cost:

Date Completed:

Shawna M.

Yield:

Cost:

Searcher's Name:

Shawna M.

Yield:

Cost:

Searcher's Title:

Shawna M.

Yield:

Cost:

Author Search

=> FILE HCAPLUS
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FILE COVERS 1907 - 11 Apr 2008 VOL 148 ISS 16
FILE LAST UPDATED: 10 Apr 2008 (20080410/ED)

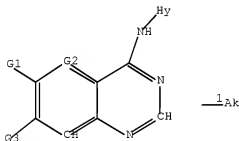
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=> D QUE L13

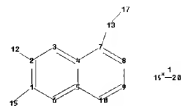
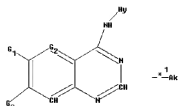
L1

STR



G1 O,S
G2 CH,[@1]
G3 H,X,Ak

Structure attributes must be viewed using STN Express query preparation:
Uploading strA.str



```

chain nodes :
12 13 15 17 19 20
ring nodes :
1 2 3 4 5 6 7 8 9 10
chain bonds :
1-15 2-12 7-13 13-17 19-20
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10
exact/norm bonds :
1-2 1-6 1-15 2-3 2-12 3-4 4-5 4-7 5-6 5-10 7-8 7-13 8-9 9-10 13-17
19-20

```

G1:O,S

G2:CH, [*1]

G3:H,X,Ak

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
12:CLASS 13:CLASS 15:CLASS 17:Atom 19:CLASS 20:CLASS
Generic attributes :
17:
Saturation : Unsaturated

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Element Count :
Node 17: Limited
N,N1

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L3      150 SEA FILE=REGISTRY SSS FUL L1
L4      6 SEA FILE=HCAPLUS ABB=ON PLU=ON L3

```

Serial No.:10/593,540

L5 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 AND (PRY<=2005 OR AY<=2005
 OR PY<=2005)
 L6 138 SEA FILE=HCAPLUS ABB=ON PLU=ON MITSUYA M2/AU
 L7 47 SEA FILE=HCAPLUS ABB=ON PLU=ON BAMBIA M2/AU
 L8 7626 SEA FILE=HCAPLUS ABB=ON PLU=ON SASAKI Y2/AU
 L9 6232 SEA FILE=HCAPLUS ABB=ON PLU=ON NISHIMURA T2/AU
 L10 19 SEA FILE=HCAPLUS ABB=ON PLU=ON EIKI J2/AU
 L11 1742 SEA FILE=HCAPLUS ABB=ON PLU=ON ARAKAWA K2/AU
 L12 15764 SEA FILE=HCAPLUS ABB=ON PLU=ON (L6 OR L7 OR L8 OR L9 OR L10
 OR L11)
 L13 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L5 AND L12

=> FILE WPIX

FILE 'WPIX' ENTERED AT 14:36:31 ON 11 APR 2008
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FILE LAST UPDATED: 8 APR 2008 <20080408/UP>
 MOST RECENT THOMSON SCIENTIFIC UPDATE: 200823 <200823/DW>
 DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> IPC Reform backfile reclassification has been loaded to the end of
 November 2007. No update date (UP) has been created for the
 reclassified documents, but they can be identified by
 20060101/UPIC and 20061231/UPIC, 20070601/UPIC, 20071001/UPIC and
 20071130/UPIC. <<<

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http://www.stn-international.com/archive/presentations/DWPIAnaVist2_0710.pdf

>>> XML document distribution format now available - See HELP XMLDOC <<<

>>> ECLA Codes and Current US National Classifications have been added -
 see NEWS and HELP CHANGE <<<

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

>>> Updated PDF files in the following links:

http://www.stn-international.de/stndatabases/details/ico_0803.zip

http://www.stn-international.de/stndatabases/details/epc_0803.zip

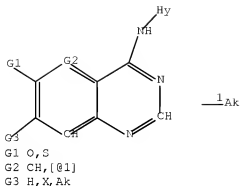
Supplement of all changed ECLA items:

http://www.stn-international.de/stndatabases/details/ecla_0803s.zip <<<

'BI,ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> D QUE L17

L1 STR



Structure attributes must be viewed using STN Express query preparation.

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L7      47  SEA FILE=HCAPLUS ABB=ON  PLU=ON  BAMBA M?/AU
L8      7626 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SASAKI Y?/AU
L9      6232 SEA FILE=HCAPLUS ABB=ON  PLU=ON  NISHIMURA T?/AU
L10     19   SEA FILE=HCAPLUS ABB=ON  PLU=ON  EIKI J?/AU
L11     1742 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ARAKAWA K?/AU
L12     15764 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L6 OR L7 OR L8 OR L9 OR L10
OR L11)
L15     63   SEA FILE=WPIX SSS FUL L1
L16     2    SEA FILE=WPIX ABB=ON  PLU=ON  L15/DCR
L17     1    SEA FILE=WPIX ABB=ON  PLU=ON  L12 AND L16
```

=> DUP REM L13 L17

FILE 'HCAPLUS' ENTERED AT 14:36:40 ON 11 APR 2008

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PROCESSING COMPLETED FOR L13

PROCESSING COMPLETED FOR L17

L22 1 DUP REM L13 L17 (1 DUPLICATE REMOVED)

ANSWER '1' FROM FILE HCAPLUS

=> D IBIB ED ABS FHITSTR L22 1

L22 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2005:1042235 HCAPLUS Full-text

DOCUMENT NUMBER: 143:347192

TITLE: Preparation of substituted quinazoline and pyridopyrimidine derivatives as glucokinase activators

INVENTOR(S): Mitsuya, Morihiro; Bamba, Makoto; Sasaki, Yasuhiro; Nishimura, Teruyuki

PATENT ASSIGNEE(S): Eiki, Junichi; Arakawa, Keisuke Banyu Pharmaceutical Co., Ltd, Japan

SOURCE: PCT Int. Appl., 192 pp.

CODEN: PIXXD2

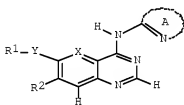
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005090332	A1	20050929	WO 2005-JP5991	20050323 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005223610	A1	20050929	AU 2005-223610	20050323 <--
CA 2560286	A1	20050929	CA 2005-2560286	20050323 <--
EP 1734040	A1	20061220	EP 2005-721640	20050323 <--
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, LV				
CN 1934100	A	20070321	CN 2005-80009447	20050323 <--
IN 2006DN05151	A	20070803	IN 2006-DN5151	20060907 <--
US 20080032996	A1	20080207	US 2007-593540	20070510 <--
PRIORITY APPLN. INFO.:			JP 2004-85808	A 20040323 <--
			WO 2005-JP5991	W 20050323 <--

OTHER SOURCE(S): MARPAT 143:347192
ED Entered STIN: 29 Sep 2005
GI



I

AB The title compds. I [X is a nitrogen atom, CH; Y is O, S; R1 is an optionally substituted 5 to 6-membered heteroaryl group, aryl, alkyl, etc.; R2 is a hydrogen atom or a fluorine atom; and the ring A is an optionally substituted monocyclic or bicyclic heteroaryl group] are prepared Thus, [6-(4H-[1,2,4]triazol-3-ylsulfanyl)quinazolin-4-yl]thiazolo[5,4-b]pyridin-2-ylamine was prepared in 2 steps from 4-chloro-6-iodoquinazoline and thiazolo[5,4-b]pyridin-2-ylamine. In a test for glucokinase activating activity, compds. of this invention showed EC50 values of 0.08 μ M to 0.18 μ M. Formulations are given.

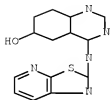
IT 865662-62-0P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of substituted quinazoline and pyridopyrimidine derivs. as glucokinase activators)

RN 865662-62-0 HCAPLUS

CN 6-Quinazolinol, 4-(thiazolo[5,4-b]pyridin-2-ylamino)- (CA INDEX NAME)



ONE OR MORE TAUTOMERIC DOUBLE BONDS NOT DISPLAYED IN THE STRUCTURE

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Serial No.:10/593,540
Structure Search

=> FILE HCAPLUS
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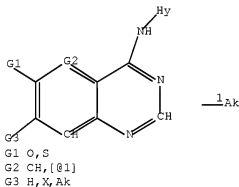
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FILE COVERS 1907 - 11 Apr 2008 VOL 148 ISS 16
FILE LAST UPDATED: 10 Apr 2008 (20080410/ED)

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=> D QUE L5
L1 STR



Structure attributes must be viewed using STN Express query preparation.
L3 150 SEA FILE=REGISTRY SSS FUL L1
L4 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L3
L5 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L4 AND (PRY<=2005 OR AY<=2005
OR PY<=2005)

=> S L5 NOT L13
L23 5 L5 NOT L13

=> FILE WPIX

FILE 'WPIX' ENTERED AT 14:37:14 ON 11 APR 2008

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FILE LAST UPDATED: 8 APR 2008 <20080408/UP>

MOST RECENT THOMSON SCIENTIFIC UPDATE: 200823 <200823/DW>

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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http://www.stn-international.com/archive/presentations/DWPIAnaVist2_0710.pdf

>>> XML document distribution format now available - See HELP XMLDOC <<<

>>> ECLA Codes and Current US National Classifications have been added - see NEWS and HELP CHANGE <<<

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

>>> Updated PDF files in the following links:

http://www.stn-international.de/stndatabases/details/ico_0803.zip

http://www.stn-international.de/stndatabases/details/epc_0803.zip

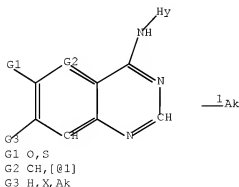
Supplement of all changed ECLA items:

http://www.stn-international.de/stndatabases/details/ecla_0803s.zip <<<

'BI,ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> D QUE L16

L1 STR



Structure attributes must be viewed using STN Express query preparation.

L15 63 SEA FILE=WPIX SSS FUL L1
 L16 2 SEA FILE=WPIX ABB=ON PLU=ON L15/DCR

=> S L16 NOT L17
 L24 1 L16 NOT L17

=> FILE BABS
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FILE LAST UPDATED: 17 MAR 2008 <20080317/UP>
 FILE COVERS 1980 TO DATE.

=> D QUE L20
 L20 1 SEA FILE=BABS ABB=ON PLU=ON 6424720/BABSAN

=> FILE BEILSTEIN
 FILE 'BEILSTEIN' ENTERED AT 14:37:44 ON 11 APR 2008
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FILE LAST UPDATED ON April 1, 2008

FILE COVERS 1771 TO 2008.
 *** FILE CONTAINS 10.322,808 SUBSTANCES ***

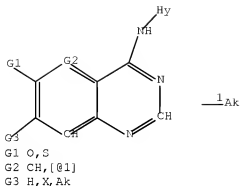
>>>PLEASE NOTE: Reaction Data and substance data are stored in
 separate documents and can not be searched together in one query.
 Reaction data for BEILSTEIN compounds may be displayed
 immediately with the display codes PRE (preparations) and REA
 (reactions). A substance answer set retrieved after the search
 for a chemical name, a compounds with available reaction
 information by combining with PRE/FA, REA/FA or more generally
 with RX/FA. The BEILSTEIN Registry Number (BRN) is the link
 between a BEILSTEIN compound and belonging reactions. For mo
 detailed reaction searches BRNs can be searched as reaction
 partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

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 * ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. *
 * FOR PRICE INFORMATION SEE HELP COST *

>>> Price change as of January 1st, 2008: Connect Time and Structure
 Search fees re-introduced. See NEWS and HELP COST <<<

=> D QUE L21
 L1 STR



Structure attributes must be viewed using STN Express query preparation.

L18 4 SEA FILE=BEILSTEIN SSS FUL L1
L19 1 SEA FILE=BEILSTEIN ABB=ON PLU=ON L18 AND BABSAN/FA
L21 3 SEA FILE=BEILSTEIN ABB=ON PLU=ON L18 NOT L19

=> DUP REM L23 L24 L20 L21

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PROCESSING COMPLETED FOR L23

PROCESSING COMPLETED FOR L24

PROCESSING COMPLETED FOR L20

PROCESSING COMPLETED FOR L21

L25 8 DUP REM L23 L24 L20 L21 (2 DUPLICATES REMOVED)

ANSWERS '1-5' FROM FILE HCAPLUS

ANSWERS '6-8' FROM FILE BEILSTEIN

=> D IBIB ED ABS HITSTR 1-5; D IDE ALLREF 6-8

L25 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2003:981459 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:228690

TITLE:

Synthesis and SAR of potent EGFR/erbB2 dual inhibitors

AUTHOR(S): Zhang, Yue-Mei; Cockerill, Stuart; Guntrip, Stephen

B.; Rusnak, David; Smith, Kathryn; Vanderwall, Dana;

Wood, Edgar; Lackey, Karen

CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709,

SOURCE: USA
Bioorganic & Medicinal Chemistry Letters (2004), 14(1), 111-114
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

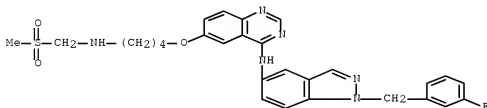
ED Entered STN: 17 Dec 2003

AB A series of 6-alkoxy-4-anilinoquinazoline compds. was prepared and evaluated for in vitro inhibition of the erbB2 and EGFR kinase activity. The IC50 values of the best compds. were below 0.10 uM. Further, several of these compds. inhibit the growth of erbB2 and EGFR over-expressing tumor cell lines at concns. below 1 uM.

IT 568437-13-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and structure-activity relations of potent EGFR/erbB2 kinase dual inhibitors)

RN 668437-13-6 HCAPLUS

CN 4-Quinazolinamine, N-[1-[(3-fluorophenyl)methyl]-1H-indazol-5-yl]-6-[4-[(methylsulfonyl)methyl]amino]butoxy]- (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 1999:451283 HCAPLUS Full-text

DOCUMENT NUMBER: 131:102287

TITLE: Preparation of quinazolinylamines and analogs as protein tyrosine kinase inhibitors

INVENTOR(S): Cockerill, George Stuart; Lackey, Karen Elizabeth

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

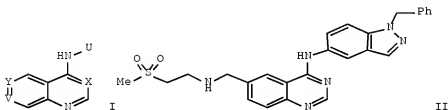
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9935132	A1	19990715	WO 1999-GB76	19990111 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,				

Serial No.:10/593,540

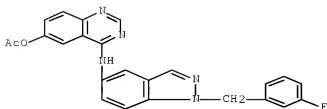
TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
 TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 AU 9919786 A 19990726 AU 1999-19786 19990111 <--
 PRIORITY APPLN. INFO.: GB 1998-575 A 19980112 <--
 WO 1999-GB76 W 19990111 <--
 OTHER SOURCE(S): MARPAT 131:102287
 ED Entered STN: 23 Jul 1999
 GI



AB Substituted heteroarom. compds. I are prepared [wherein X = N or CH; Y = CR1 and V = N; or Y = N and V = CR1; or Y = CR1 and V = CR2; or Y = CR2 and V = CR1; R1 = Q-M-, wherein M = C1-5 alkylene where any C atom not immediately adjacent to Q may be replaced by O, S, or NR6; Q = wide variety of groups; R2 = H, halo, OH, alkyl, alkoxy, (di)alkylamino; U = Ph, pyridyl, pyrimidinyl, imidazolyl, or 9- or 10-membered bicyclic heterocyclyl containing 1-2 N atoms and 0-1 addnl. O, N, or S; U is substituted by R3, where R3 = benzyl, halobenzyl, pyridylmethyl, pyridylmethoxy, PhO, PhSO2, (un)substituted phthalimido; R6 = H, alkyl]. Twelve examples and a variety of intermediates were prepared For instance, 4-chloro-6-iodoquinazoline was aminated in the 4-position with 5-amino-1-benzyl-1H-indazole, followed by Pd-catalyzed carbonylation, to give 4-[(1-benzyl-1H-indazol-5-yl)amino]quinazoline-6-carbaldehyde. This underwent reductive amination by MeSO2CH2CH2NH2 and a reducing agent such as NaBH(OAc)3, to give title compound II.HCl. In an EGFR phosphorylation assay, II.HCl had an IC50 of <0.10 μM.

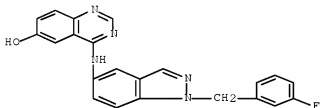
IT 236955-59-6P 230955-69-9P 230955-73-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (intermediate; preparation of quinazolinylamines and analogs as protein tyrosine kinase inhibitors)

RN 230955-59-6 HCAPLUS
 CN 6-Quinazolinol, 4-[[1-[(3-fluorophenyl)methyl]-1H-indazol-5-yl]amino]-, acetate (ester) (9CI) (CA INDEX NAME)



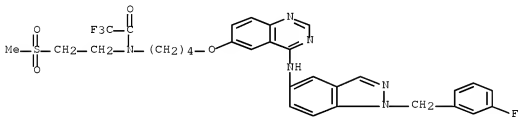
RN 230955-60-9 HCAPLUS

CN 6-Quinazolinol, 4-[[1-[(3-fluorophenyl)methyl]-1H-indazol-5-yl]amino]-
(CA INDEX NAME)



RN 230955-73-4 HCAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[4-[[4-[[1-[(3-fluorophenyl)methyl]-1H-indazol-5-yl]amino]-6-quinazolinyl]oxy]butyl]-N-[2-(methylsulfonyl)ethyl]-
(CA INDEX NAME)

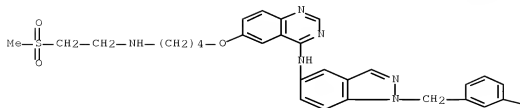


IT 230955-49-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of quinazolinylamines and analogs as protein tyrosine kinase inhibitors)

RN 230955-49-4 HCAPLUS

CN 4-Quinazolinamine, N-[1-[(3-fluorophenyl)methyl]-1H-indazol-5-yl]-6-[[4-[[2-(methylsulfonyl)ethyl]amino]butoxy]- (CA INDEX NAME)



F

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:743253 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 136:79264

TITLE: The characterization of novel, dual ErbB-2/EGFR, tyrosine kinase inhibitors: potential therapy for cancer

AUTHOR(S): Rusnak, David W.; Affleck, Karen; Cockerill, Stuart G.; Stubberfield, Colin; Harris, Robert; Page, Martin; Smith, Kathryn J.; Guntrip, Stephen B.; Carter, Malcolm C.; Shaw, Robert J.; Jowett, Amanda; Stables, Jeremy; Topley, Peter; Wood, Edgar R.; Brignola, Perry S.; Kadwell, Sue H.; Reep, Bryan R.; Mullin, Robert J.; Alligood, Krystal J.; Keith, Barry R.; Crosby, Renae M.; Murray, Doris M.; Knight, W. Blaine; Gilmer, Tona M.; Lackey, Karen

CORPORATE SOURCE: Department of Cancer Biology, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA

SOURCE: Cancer Research (2001), 61(19), 7196-7203
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 11 Oct 2001

AB The type 1 receptor tyrosine kinases constitute a family of transmembrane proteins involved in various aspects of cell growth and survival and have been implicated in the initiation and progression of several types of human malignancies. The best characterized of these proteins are the epidermal growth factor receptor (EGFR) and ErbB-2 (HER-2/neu). We have developed potent quinazoline and pyrido-[3,4-d]-pyrimidine small molcs. that are dual inhibitors of ErbB-2 and EGFR. The compds. demonstrate potent in vitro inhibition of the ErbB-2 and EGFR kinase domains with IC50s <80 nM. Growth of

ErbB-2- and EGFR-expressing tumor cell lines is inhibited at concns. <0.5 μ M. Selectivity for tumor cell growth inhibition vs. normal human fibroblast growth inhibition ranges from 10- to >75-fold. Tumor growth in mouse s.c. xenograft models of the BT474 and HN5 cell lines is inhibited in a dose-responsive manner using oral doses of 10 and 30 mg/kg twice per day. In addition, the tested compds. caused a reduction of ErbB-2 and EGFR autophosphorylation in tumor fragments from these xenograft models. These data indicate that these compds. have potential use as therapy in the broad population of cancer patients overexpressing ErbB-2 and/or EGFR.

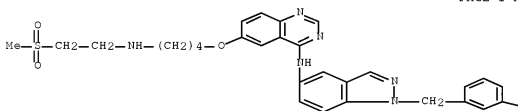
IT 230955-49-4, GW 5945

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of novel, dual ErbB-2/EGFR, tyrosine kinase inhibitors and potential therapy for cancer)

RN 230955-49-4 HCAPLUS

CN 4-Quinazolinamine, N-[1-[(3-fluorophenyl)methyl]-1H-indazol-5-yl]-6-[4-[[2-(methylsulfonyl)ethyl]amino]butoxy]- (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2008 ACS ON STN

ACCESSION NUMBER: 1999:113672 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 130:182476

TITLE: Preparation of heterocyclic compounds as irreversible bicyclic inhibitors of tyrosine kinases

INVENTOR(S): Bridges, Alexander James

PATENT ASSIGNEE(S): Warner-Lambert Company, USA

SOURCE: PCT Int. Appl., 131 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

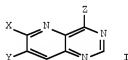
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906396	A1	19990211	WO 1998-US15592	19980729 <--
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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9886659	A	19990222	AU 1998-86659	19980729 <--
US 6153617	A	20001128	US 1999-269647	19990325 <--
US 20030087881	A1	20030508	US 2002-272651	20021017 <--
PRIORITY APPLN. INFO.:				
			US 1997-54061P	P 19970729 <--
			WO 1998-US15592	W 19980729 <--
			US 1999-269647	A3 19990325 <--
			US 2000-656331	B1 20000906 <--

OTHER SOURCE(S): MARPAT 130:182476

ED Entered STN: 19 Feb 1999

GI



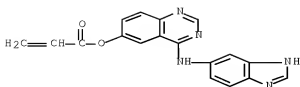
AB The title compds., e.g. I [X = DEF, Y = SR₄, etc.; or X = SR₄, etc., and Y = DEF; D = O, etc.; E = CO, etc.; F = CR₁(:C):C(R₅)H, etc.; a proviso is given; R₁ = H, halo, etc.; R₅ = H, halo, perfluoroalkyl, etc.; Z = indoline moiety (generic structure given), etc.; R₄ = H, alkyl, etc.], are prepared This invention also provides a method of treating cancer, restenosis, atherosclerosis, endometriosis, and psoriasis and a pharmaceutical composition that comprises a compound that is an irreversible inhibitor of tyrosine kinases. N-[4-(6-bromo-2,3-dihydroindol-1-yl)quinazolin-6-yl]acrylamide in vitro showed IC₅₀ of 0.4 nM against epidermal growth factor receptor tyrosine kinase.

IT 220577-65-1P 220577-66-2P 220577-73-1P
220577-74-2P 220577-75-3P 220577-76-4P
220577-77-5P 220577-78-6P 220577-79-7P
220577-80-8P 220577-82-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as irreversible bicyclic inhibitors of tyrosine kinases)

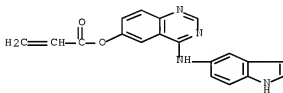
RN 220577-65-1 HCAPLUS

CN 2-Propenoic acid, 4-(1H-benzimidazol-5-ylamino)-6-quinazolinyl ester (9CI)
(CA INDEX NAME)



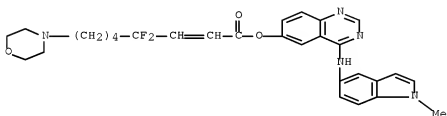
RN 220577-66-2 HCAPLUS

CN 2-Propenoic acid, 4-(1H-indol-5-ylamino)-6-quinazolinyl ester (CA INDEX NAME)



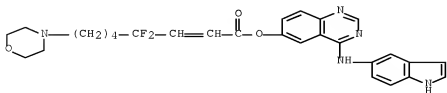
RN 220577-73-1 HCAPLUS

CN 2-Octenoic acid, 4,4-difluoro-8-(4-morpholinyl)-, 4-[(1-methyl-1H-indol-5-yl)amino]-6-quinazolinyl ester (CA INDEX NAME)



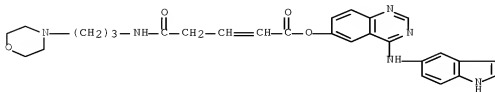
RN 220577-74-2 HCAPLUS

CN 2-Octenoic acid, 4,4-difluoro-8-(4-morpholinyl)-, 4-(1H-indol-5-ylamino)-6-quinazolinyl ester (CA INDEX NAME)



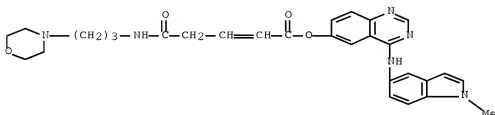
RN 220577-75-3 HCAPLUS

CN 2-Pentenoic acid, 5-[[3-(4-morpholinyl)propyl]amino]-5-oxo-,
4-(1H-indol-5-ylamino)-6-quinazoliny ester (CA INDEX NAME)



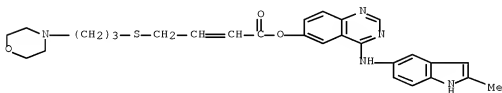
RN 220577-76-4 HCAPLUS

CN 2-Pentenoic acid, 5-[[3-(4-morpholinyl)propyl]amino]-5-oxo-,
4-[(1-methyl-1H-indol-5-yl)amino]-6-quinazoliny ester (CA INDEX NAME)



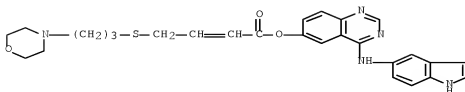
RN 220577-77-5 HCAPLUS

CN 2-Butenoic acid, 4-[[3-(4-morpholinyl)propyl]thio]-, 4-[(2-methyl-1H-indol-5-yl)amino]-6-quinazoliny ester (CA INDEX NAME)



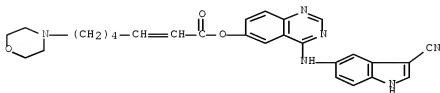
RN 220577-78-6 HCAPLUS

CN 2-Butenoic acid, 4-[[3-(4-morpholinyl)propyl]thio]-, 4-(1H-indol-5-ylamino)-6-quinazoliny ester (CA INDEX NAME)



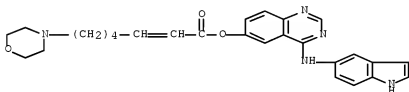
RN 220577-79-7 HCAPLUS

CN 2-Heptenoic acid, 7-(4-morpholinyl)-, 4-[(3-cyano-1H-indol-5-yl)amino]-6-quinazolinyl ester (CA INDEX NAME)



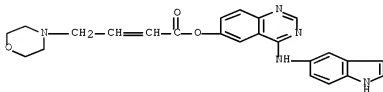
RN 220577-80-0 HCAPLUS

CN 2-Heptenoic acid, 7-(4-morpholinyl)-, 4-(1H-indol-5-ylamino)-6-quinazolinyl ester (CA INDEX NAME)



RN 220577-82-2 HCAPLUS

CN 2-Butenoic acid, 4-(4-morpholinyl)-, 4-(1H-indol-5-ylamino)-6-quinazolinyl ester (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2008 ACS ON STN
 ACCESSION NUMBER: 1995:23238 HCAPLUS [Full-text](#)
 DOCUMENT NUMBER: 122:31545

TITLE: Preparation of aminoquinazolines useful in the treatment of cancer

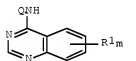
INVENTOR(S): Barker, Andrew John; Brown, Dearg Sutherland
 PATENT ASSIGNEE(S): Zeneca, UK

SOURCE: Eur. Pat. Appl., 39 pp.

DOCUMENT TYPE: CODEN: EPXXDW
 LANGUAGE: Patent
 FAMILY ACC. NUM. COUNT: English
 PATENT INFORMATION: 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 602851	A1	19940622	EP 1993-309680	19931203 <--
EP 602851	B1	19961009		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AU 9350728	A	19940623	AU 1993-50728	19931116 <--
AU 664496	B2	19951116		
ZA 9308594	A	19940610	ZA 1993-8594	19931117 <--
CA 2103383	A1	19940611	CA 1993-2103383	19931118 <--
CA 2103383	C	20050125		
IL 107678	A	19990312	IL 1993-107678	19931119 <--
HU 65622	A2	19940728	HU 1993-3328	19931124 <--
FI 9305431	A	19940611	FI 1993-5431	19931203 <--
AT 143956	T	19961015	AT 1993-309680	19931203 <--
ES 2093367	T3	19961216	ES 1993-309680	19931203 <--
CZ 283612	B6	19980513	CZ 1993-2651	19931206 <--
NO 9304504	A	19940613	NO 1993-4504	19931209 <--
JP 06336481	A	19941206	JP 1993-309184	19931209 <--
JP 3330706	B2	20020930		
CN 1094043	A	19941026	CN 1993-120872	19931210 <--
US 5580870	A	19961203	US 1993-164725	19931210 <--
PRIORITY APPLN. INFO.:			GB 1992-25765	A 19931210 <--
			GB 1993-10248	A 19930518 <--

OTHER SOURCE(S): MARPAT 122:31545
 ED Entered STN: 08 Nov 1994
 GI

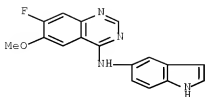


AB The title compds. [I; Q = 9- or 10-membered bicyclic heterocyclic moiety containing 1-2 N atoms; R1 = OH, NH2, ureido, hydroxyamino, trifluoromethoxy, (un)substituted C1-4 alkyl, C1-4 alkoxy, pyrrolidin-1-yl, piperidino, etc.; m = 1-3], useful in the treatment of cancer (no data), are prepared and I- containing formulations presented. Thus, 4-chloro-6,7- dimethoxyquinazoline was reacted with 5-aminoquinoline, producing 6,7-dimethoxy-4-(5-quinolylamino)quinazoline, m.p. > 240°, in 35% yield.

IT 159768-49-7P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of, as anticancer agent)

RN 159768-49-7 HCAPLUS

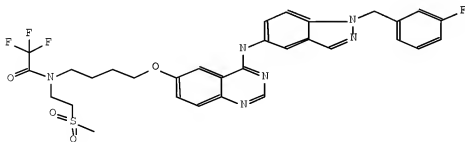
CN 4-Quinazolinamine, 7-fluoro-N-1H-indol-5-yl-6-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L25 ANSWER 6 OF 8 BEILSTEIN COPYRIGHT 2008 BEILSTEIN MDL on STN

Beilstein Records (BRN):	9602965
Chemical Name (CN):	2,2,2-trifluoro-N-(4-(4-(1-(3-fluoro-benzyl)-1H-indazol-5-ylamino)-quinazolin-6-yloxy)-butyl)-N-(2-methanesulfonyl-ethyl)-acetamide
Autonom Name (AUN):	2,2,2-trifluoro-N-(4-(4-(1-(3-fluoro-benzyl)-1H-indazol-5-ylamino)-quinazolin-6-yloxy)-butyl)-N-(2-methanesulfonyl-ethyl)-acetamide
Molec. Formula (MF):	C31 H30 F4 N6 O4 S
Molecular Weight (MW):	658.67
Lawson Number (LN):	29684, 29566, 16445, 3140, 3125, 1157, 292
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	8097768
Tautomer ID (TAUTID):	9008192
Entry Date (DED):	2004/04/23
Update Date (DUPD):	2004/04/23



Field Availability:

Code Name

Occurrence

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BRN      Beilstein Records      1
CN       Chemical Name          1
AUN      Autonomname            1
MF       Molecular Formula      1
FW       Formular Weight        1
LN       Lawson Number          7
CTYPE    Compound Type          1
CONSID   Constitution ID        1
TAUTID   Tautomer ID            1
ED       Entry Date              1
UPD      Update Date             1

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This substance also occurs in Reaction Documents:

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Code      Name                      Occurrence
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RX        Reaction Documents        2
RXREA     Substance is Reaction Reactant  1
RXPRO     Substance is Reaction Product   1

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All References:

ALLREF

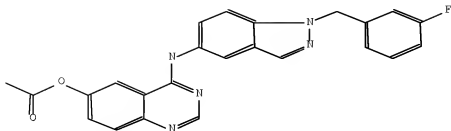
1. Zhang, Yue-Mei; Cockerill, Stuart; Guntrip, Stephen B.; Rusnak, David; Smith, Kathryn; Vanderwall, Dana; Wood, Edgar; Lackey, Karen, Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 14(1), <2004>, 111 - 114; BABS-6424720

L25 ANSWER 7 OF 8 BEILSTEIN COPYRIGHT 2008 BEILSTEIN MDL on STN

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Beilstein Records (BRN):      9589052
Chemical Name (CN):          acetic acid 4-<1-(3-fluoro-benzyl)-1H-
                               indazol-5-ylamino>-quinazolin-6-yl ester
Autonom Name (AUN):          acetic acid 4-<1-(3-fluoro-benzyl)-1H-
                               indazol-5-ylamino>-quinazolin-6-yl ester
Molec. Formula (MF):          C24 H18 F N5 O2
Molecular Weight (MW):        427.44
Lawson Number (LN):          29684, 29566, 16445, 1155
Compound Type (CTYPE):        heterocyclic
Constitution ID (CONSID):     8086336
Tautomer ID (TAUTID):         9002439
Entry Date (DED):             2004/04/23
Update Date (DUPD):           2004/04/23

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Field Availability:

Code	Name	Occurrence
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AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	4
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	2
RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

All References:

ALLREF

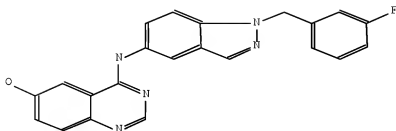
1. Zhang, Yue-Mei; Cockerill, Stuart; Guntrip, Stephen B.; Rusnak, David; Smith, Kathryn; Vanderwall, Dana; Wood, Edgar; Lackey, Karen, Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 14(1), <2004>, 111 - 114; BABS-6424720

L25 ANSWER 8 OF 8 BEILSTEIN COPYRIGHT 2008 BEILSTEIN MDL on STN

Beilstein Records (BRN): 9584302
 Chemical Name (CN): 4-<1-(3-fluoro-benzyl)-1H-indazol-5-ylamino>-quinazolin-6-ol
 Autonom Name (AUN): 4-<1-(3-fluoro-benzyl)-1H-indazol-5-ylamino>-quinazolin-6-ol
 Molec. Formula (MF): C22 H16 F N5 O
 Molecular Weight (MW): 385.40
 Lawson Number (LN): 29684, 29566, 16445
 Compound Type (CTYPE): heterocyclic
 Constitution ID (CONSID): 8082402

Serial No.:10/593,540

Tautomer ID (TAUTID): 8997062
 Entry Date (DED): 2004/04/23
 Update Date (DUPD): 2004/04/23



Field Availability:

Code	Name	Occurrence
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CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	3
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	2
RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

All References:

ALLREF

1. Zhang, Yue-Mei; Cockerill, Stuart; Guntrip, Stephen B.; Rusnak, David; Smith, Kathryn; Vanderwall, Dana; Wood, Edgar; Lackey, Karen, Bioorg.Med.Chem.Lett., CODEN: BMCL8, 14(1), <2004>, 111 - 114; BABS-6424720

Search History

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L1          STRUCTURE UPLOADED
L2          12 SEA SSS SAM L1
L3          150 SEA SSS FUL L1

FILE 'HCAPLUS' ENTERED AT 14:26:51 ON 11 APR 2008
L4          6 SEA ABB=ON PLU=ON L3
L5          6 SEA ABB=ON PLU=ON L4 AND (PRY<=2005 OR AY<=2005 OR PY<=2005)

L6          138 SEA ABB=ON PLU=ON MITSUYA M?/AU
L7          47 SEA ABB=ON PLU=ON BAMBA M?/AU
L8          7626 SEA ABB=ON PLU=ON SASAKI Y?/AU
L9          6232 SEA ABB=ON PLU=ON NISHIMURA T?/AU
L10         19 SEA ABB=ON PLU=ON EIKI J?/AU
L11         1742 SEA ABB=ON PLU=ON ARAKAWA K?/AU
L12         15764 SEA ABB=ON PLU=ON (L6 OR L7 OR L8 OR L9 OR L10 OR L11)
L13         1 SEA ABB=ON PLU=ON L5 AND L12

FILE 'WPIX' ENTERED AT 14:29:28 ON 11 APR 2008
L14         8 SEA SSS SAM L1
L15         63 SEA SSS FUL L1
L16         2 SEA ABB=ON PLU=ON L15/DCR
L17         1 SEA ABB=ON PLU=ON L12 AND L16

FILE 'BEILSTEIN' ENTERED AT 14:33:40 ON 11 APR 2008
L18         4 SEA SSS FUL L1
          SEL BABSAN
L19         1 SEA ABB=ON PLU=ON L18 AND BABSAN/FA
          SEL BABSAN

FILE 'BABS' ENTERED AT 14:34:55 ON 11 APR 2008
L20         1 SEA ABB=ON PLU=ON 6424720/BABSAN

FILE 'BEILSTEIN' ENTERED AT 14:35:08 ON 11 APR 2008
L21         3 SEA ABB=ON PLU=ON L18 NOT L19

FILE 'HCAPLUS, WPIX' ENTERED AT 14:36:40 ON 11 APR 2008
L22         1 DUP REM L13 L17 (1 DUPLICATE REMOVED)

FILE 'HCAPLUS' ENTERED AT 14:36:58 ON 11 APR 2008
          D QUE L5
L23         5 SEA ABB=ON PLU=ON L5 NOT L13

FILE 'WPIX' ENTERED AT 14:37:14 ON 11 APR 2008
L24         1 SEA ABB=ON PLU=ON L16 NOT L17

FILE 'HCAPLUS, WPIX, BABS, BEILSTEIN' ENTERED AT 14:37:59 ON 11 APR 2008
L25         8 DUP REM L23 L24 L20 L21 (2 DUPLICATES REMOVED)

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